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COMPARATIVE EFFECTS OF HYPEROXIA AND HYPERBARIC PRESSURE IN TREATMENT OF PRIMARY BLAST INJURY

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Guinea pigs and rabbits were exposed to lethal reflected pressures in an air-driven shock tube and were subsequently treated in a hyperbaric chamber in which the oxygen tension (P_{O_2}) and chamber pressure were independently varied. Treatments involving increases in P_{O_2} resulted in increased survival times of guinea pigs whereas pressurization for 30 minutes at 36 or 72 p.s.i.g. with the P_{O_2} retained at the normal ambient level by use of an N_2-air mixture had no detectable effect on survival times of the animals. To study the effects of prolonged hyperbaric oxygenation in treatment of blast injury, guinea pigs and rabbits were treated on a 29-hour schedule having an initial 3-hour hold-time at the pressure-treatment level followed by 26 hours for decompression. In rabbits, an initial P_{O_2} of 17.5 p.s.i.a., achieved either by air pressure at 72 p.s.i.g. or by pressurization to 15 p.s.i.g. with 65-percent O_2, 35-percent N_2, resulted in full survival and recovery of all treated animals. In guinea pigs, treatment with 100-percent O_2 at 5.5 p.s.i.g. (P_{O_2} = 17.5 p.s.i.a.) or at 12 p.s.i.g. (P_{O_2} = 24 p.s.i.a.) resulted in increased survival times with no increase in overall survival and recovery in the first case and significantly increased survival and recovery compared to that of untreated controls in the second case. The pathophysiology of primary blast injury is discussed with special reference to the roles of air embolism and cardiopulmonary pathology in the etiology of death.

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FOREWORD

This report presents the results of initial studies designed to establish a therapeutic regimen for the treatment of primary direct airblast injury. It describes experiments designed to assess the effects of hyperbaric treatment of blast injury with special reference to the effects of hyperoxia compared to pressurization without increased oxygenation in treatment of blast-injured guinea pigs and rabbits.

The findings may be of interest to those involved in the treatment of chest injuries, the analysis of weapons effects, or in industrial or military medicine.

This study is a part of a broad program in the field of blast and shock biology designed to obtain data for use in prediction of hazards from explosions and in the development of a sound basis for the prognosis and treatment of blast injuries.

ABSTRACT

Guinea pigs and rabbits were exposed to lethal, reflected pressures in an air-driven shock tube and were subsequently treated in a hyperbaric chamber in which the oxygen tension (P_{O_2}) and chamber pressure were independently varied. Treatments involving increases in P_{O_2} resulted in increased survival times of guinea pigs whereas pressurization for 30 minutes at 36 or 72 p.s.i.g. with the P_{O_2} retained at the normal ambient level by use of an N_2-air mixture had no detectable effect on survival times of the animals.

To study the effects of prolonged hyperbaric oxygenation in treatment of blast injury, guinea pigs and rabbits were treated on a 29-hour schedule having an initial 3-hour hold at the pressure-treatment level followed by 26 hours for decompression. In rabbits, an initial P_{O_2} of 17.5 p.s.i.a., achieved either by air pressure at 72 p.s.i.g. or by pressurization to 15 p.s.i.g. with 65-percent O_2, 35-percent N_2, resulted in full survival and recovery of all treated animals. In guinea pigs, treatment with 100-percent O_2 at 5.5 p.s.i.g. (P_{O_2} = 17.5 p.s.i.a.) or at 12 p.s.i.g. (P_{O_2} = 24 p.s.i.a.) resulted in increased survival times with no increase in overall survival and recovery in the first case and significantly increased survival and recovery compared to that of untreated controls in the second case.

The pathophysiology of primary blast injury is discussed with special reference to the roles of air embolism and cardiopulmonary pathology in the etiology of death.

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Also, the senior author would like to express sincere appreciation to Dr. Donald R. Richmond for valuable consultations and encouragement during the course of this study.

The experimental work discussed in this manuscript was conducted according to the principles enunciated in the "Guide for Laboratory Animal Facilities and Care," prepared by the National Academy of Sciences-National Research Council.

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COMPARATIVE EFFECTS OF HYPEROXIA AND HYPERBARIC PRESSURE IN TREATMENT OF PRIMARY BLAST INJURY

Edward G. Damon and Robert K. Jones

INTRODUCTION

Acute deaths from primary blast injuries that are not accompanied by fractures or external lesions are generally attributed to a failure of circulation or respiration.[2, 3, 15, 18] Investigators have recognized three main causes of circulatory failure resulting from the direct effects of blast overpressures on the body: (1) arterial air embolism of the coronary or cerebral vessels;[3] (2) commotio cordis (i.e., direct trauma to the heart);[3, 15] and (3) acute cor pulmonale caused by a sudden increase in the pulmonary vascular resistance as a result of mechanical and reflex mediated factors in cases of severe blast lung injury.[2, 5, 15] Failure of respiration may result from (1) respiratory arrest caused by central nervous system effects which are probably secondary to air embolism; (2) suffocation due to the blocking of airways with blood clots; and (3) reduction of ventilatory capacity of the lungs beyond the limits of physiological endurance as a result of extensive intra-alveolar hemorrhage and edema resulting in increased venous admixture.[8, 9, 13] There is no general consensus concerning the relative significance of each of these factors as a major cause of death in blast injury; and, indeed in many cases, all may be contributory factors.

Previous studies have revealed a high incidence of air embolism observed at autopsy in animals exposed to fatal overpressures; and, consequently, this has been considered to be a major life-threatening hazard in blast injury.[3, 10] The air evidently enters the circulation from the disrupted tissues of the blast-injured lung and is then carried through the arterial circulation. Disorders of the central nervous system or death frequently occurs within a few minutes after the detonation as a result of cerebral or coronary air embolism. Since most of those that survive for a few hours after exposure to airblast recover from primary blast injuries, the problem of treatment for air embolism is of prime interest to those who would administer to the needs of blast-injured patients.

It has long been recognized that in cases of gas embolism resulting from decompression sickness, traumatic air embolism from explosive decompression, bends, caisson sickness, and related syndromes, the most effective therapeutic procedure known is to recompress the subject in a suitable pressure vessel until the symptoms are alleviated and follow this with slow decompression to prevent recurrence. The aims of this type of therapy are threefold: (1) Reduction in volumes of the gas bubbles, (2) Acceleration of the resolution of the bubbles, and (3) Improvement in tissue oxygenation. Whether the breathing medium is oxygen or air during hyperbaric treatment, the partial pressure of oxygen (P_{O_2}) will be elevated, thus resulting in increased oxygenation.

Although the role of air embolism as a probable major cause of death in blast injury has been recognized for more than two decades,[3] very little attention has been devoted to the effects of hyperbaric treatment in such cases. Previous studies, conducted first by Benzinger and later by Clemedson, have indicated that recompression of a dog and rabbits to 4 atmospheres (atm) positive pressure soon after exposure to lethal overpressures from high explosives resulted in increased survival time and alleviation of electrocardiographic signs of coronary insufficiency.[3, 10]

Presumably, pressurization with air might be beneficial to a blast-injured subject both because of the direct action of the pressure on the body resulting in decreases in the volumes and increase in the rate of resolution of air emboli and because of the increased oxygen tension in the pressurized environment. The latter would be beneficial in treatment of cardiac decompensation and respiratory insufficiency in addition to that of air embolism. To our knowledge, the relative effects of these two parameters, the pressure, per se, and the P_{O_2} of the treatment environment as factors affecting survival from exposure to lethal overpressure, have not been previously studied; nor have there been previous systematic investigations of the effects of pressurization to different pressure levels following airblast injury.

The purpose of this study was to investigate the relative effects of different modes of hyperbaric treatment or oxygen therapy on survival of guinea pigs and rabbits exposed to shock-tube-generated airblasts and to evaluate the relative therapeutic effects of hyperoxia compared with that of pressurization without increase in oxygenation in treatment of blast injury.

METHODS

Animals and Airblast Exposures

A total of 165 female English breed guinea pigs and 30 female New Zealand white rabbits were utilized in this study.

The animals were subjected to reflected blast pressures of "long" duration on the endplate of a 24-inch-diameter, air-driven shock tube.[20] The ambient pressure at exposure was 12 p.s.i.a.[12, 14]

Modes of Treatment

Guinea Pigs--Short-Duration Treatment

Guinea pigs, four per shot, were exposed to reflected shock-tube pressures having a mean and range of 30.6 (28.7-32.7) p.s.i.g. Two animals were randomly selected on each shot to receive hyperbaric treatment, and the other two were retained as blast controls or, in a few cases, were given oxygen treatment at normal ambient pressure. All modes of treatment began 1 minute post-shot. The pressure rise for all methods of hyperbaric treatment was at the rate of 12 p.s.i.g./10 seconds with a hold-time at the treatment level of 30 minutes and decompression at the rate of 12 p.s.i.g./10 minutes for 12- and 36-p.s.i.g. experiments, but was stepwise in accordance with the Navy decompression tables for the 72-p.s.i.g. experiments. Illustrations of the pressure-time profiles for all modes of treatment are presented in the results (Figures 1-4). A total of 58 animals were retained as blast controls, and 70, in groups of 10 each, received treatment as follows:

Phase I: Hyperbaric treatment with air at 12, 36, or 72 p.s.i.g. above the Albuquerque ambient pressure of 12 p.s.i.a.

Phase II: Pressurization to 36 or 72 p.s.i.g. with a nitrogen and air mixture such that the P_{O_2} of the treatment chamber was retained at the Albuquerque level (P_{O_2} = 2.5 p.s.i.a.).

Phase III: Treatment with 100-percent oxygen at Albuquerque ambient pressure for 4 hours (P_{O_2} = 12 p.s.i.a.).

Phase IV: Hyperbaric treatment for 30 minutes with an air-oxygen mixture at 36 p.s.i.g. with the P_{O_2} being the same as in phase III (P_{O_2} = 12 p.s.i.a.).

Comparison of the 30-minute survival of like pressure groups in phases I and II was expected to provide information on the effects of variation in the P_{O_2} when the post-shot hyperbaric pressure is held constant, and comparison of the group in phase III with that of phase IV would indicate the effects of variation in hyperbaric pressure when the P_{O_2} is held constant.

All fatalities were autopsied soon after death, and survivors were sacrificed after 48 hours.

Rabbits--Prolonged Hyperbaric Treatment

Rabbits were exposed in pairs to reflected blast pressures ranging from 26.1 to 32.2 p.s.i.g. with a mean of 28.5 p.s.i.g. One member of each pair was randomly selected to serve as an airblast control, and the other was given hyperbaric treatment beginning 2 minutes post-shot. The hyperbaric treatment schedule utilized in these experiments was modified from the Alvis and Cosgrove table for prolonged recompression treatment of traumatic air embolism.[1] In order to assess the effects of two different levels of pressure at the same P_{O_2} levels during the treatment period, the following two modes of treatment were utilized:

Treatment Group A: Seven rabbits were given hyperbaric treatment with air. The rate of pressure rise was the same as described above for guinea pigs. The total treatment time was near 29 hours with an initial hold-time of 3 hours at 72 p.s.i.g. (P_{O_2} = 17.5 p.s.i.a.). The first four decompression steps (to 35.6 p.s.i.g.) were the same as in the Alvis and Cosgrove table,[1] followed by a slow decline from 35.6 to 18.4 p.s.i.g. during 16 hours. At this point, it was considered that the tissues would be saturated with N_2 at the

13.4-p.s.i.g. level. To complete the process, decompression steps and hold-times as given in the Navy decompression table for exceptional exposures, were utilized.[23] An illustration of the resulting pressure treatment profile is presented in the results (Figure 5a).

Treatment Group B: Six rabbits were pressurized with a gas mixture of 65-percent O_2 and 35-percent N_2 to 15 p.s.i.g. (P_{O_2} = 17.5 p.s.i.a.). They were held at this level for 3 hours and decompressed in steps such that the P_{O_2} changes with time during the first 9 hours were the same as group A above. During the remaining 20 hours of the treatment period, the pressure in the chamber was retained at 0.5 p.s.i.g. and the P_{O_2} at 8.1 p.s.i.a. An illustration of this treatment profile is presented in the results (Figure 5b).

A total of 17 rabbits, 13 of which were exposed on the same shots as the treated animals, were retained as untreated blast controls. All fatalities were autopsied soon after death, and survivors were retained more than 14 days before autopsy.

Guinea Pigs--Prolonged Treatment With Hyperoxia

Two experiments were conducted to assess the effects of prolonged treatment with high-concentration, hyperbaric oxygen on survival and recovery of blast-injured guinea pigs. The total treatment time in both experiments was 29 hours beginning within 1 minute following the shot. The pressure-treatment profiles for these experiments are illustrated in figure 11 in the results.

In the first experiment, nine guinea pigs were treated with 100-percent oxygen for 6 hours followed by 65-percent O_2, and 35-percent N_2 for 23 hours. The initial P_{O_2} was 17.5 p.s.i.a. for 3 hours followed by stepwise reductions in the P_{O_2} at 1-hour intervals for the next 3 hours, at the end of which time the chamber pressure was 0.5 p.s.i.g. and the P_{O_2} was 12.5 p.s.i.a. In order to continue the reduction in the P_{O_2}, it was then necessary to change the O_2 concentration (F_{O_2}) in the chamber. For this purpose, the chamber was pressurized with 65-percent O_2, 35-percent N_2 to 4 p.s.i.g. and retained at this level for

1 hour, while the P_{O_2} was allowed to decline to 11.5 p.s.i.a. as the F_{O_2} dropped during ventilation of the chamber. The pressure in the chamber was then reduced to 0.5 p.s.i.g. and retained at this level for the remainder of the treatment period, while the P_{O_2} of the chamber leveled off at 8.1 p.s.i.a. as the F_{O_2} approached that of the inflowing 65-percent O_2, 35-percent N_2 gas mixture. These changes in the F_{O_2}, chamber pressure, and P_{O_2} are shown in figure 11a in the results.

In the second experiment, eight guinea pigs were pressurized with 100-percent O_2 to a P_{O_2} level of 24 p.s.i.a. for 3 hours. The P_{O_2} was then reduced stepwise in increments of 2 p.s.i. at 1-hour intervals for the next 4 hours. The pressure in the chamber was then retained at 2 p.s.i.g. with P_{O_2} of 14 p.s.i.a. for the next 16 hours. At this time, the P_{O_2} was again reduced stepwise in increments of 2 p.s.i. at 1-hour intervals by flushing the chamber with air and pressurizing the chamber to maintain the P_{O_2} at the desired level as the F_{O_2} of the chamber gas fell. This stepwise reduction in P_{O_2} was continued until the pressure and P_{O_2} of the chamber reached the normal ambient level at the end of the 29-hour treatment period (Figure 11b). Twenty guinea pigs which were exposed to airblast in connection with these two experiments were retained as untreated controls. The mean reflected shock pressure to which the guinea pigs in this series were exposed was 28.4 p.s.i.g. with a range of 26.8 to 30 p.s.i.g. The nonsurvivors were posted soon after death, and surviving animals were sacrificed after 14 days.

Hyperbaric Chamber

The hyperbaric chamber used in these experiments was cylindrical with an inside diameter of 18 inches, length of 36 inches, and volume of 142 liters (Model 1836, Bethlehem Corp., 225 W. Second St., Bethlehem, Pa.).

Control of moisture and carbon dioxide buildup within the chamber was achieved by use of a carbon-dioxide absorbant (Baralyme granules, Warren E. Collins, Inc., 220 Wood Rd., Braintree, Mass.) and a desiccant (Drierite, W. A. Hammon Drierite Co., Xenio, Ohio) during the short-duration guinea-pig

experiment, and by means of constant ventilation of the chamber during the prolonged rabbit and guinea-pig treatment procedures. Throughout all treatment procedures, the carbon-dioxide tension (P_{CO_2}) of gases in the chamber was retained at levels below 10-mm. Hg. The chamber gases were analyzed by the micro Scholander technique[21] and by means of a Beckman Spinco Model LB-1 CO_2 Analyzer with Linearizer and a Med. Science Electronics Model 305AR nitrogen analyzer.

For the guinea-pig experiments involving pressurization without increase in P_{O_2} (Phase II above), the animals were sealed in the chamber filled with air at normal ambient pressure and then pressurized to the treatment level with 100-percent N_2. There was no ventilation of the chamber during the 30-minute hold-period, but the O_2 consumption of the guinea pigs compared with the volume of the chamber was such that the P_{O_2} of the chamber gas slowly declined from 2.51 p.s.i. (~130-mm. Hg) to 2.45 p.s.i. (127-mm. Hg) and adjustments in the P_{O_2} were therefore not required for this 30-minute, post-shot, primary period of interest. During the decompression phase from 72 p.s.i.g., adjustments in the P_{O_2} of the chamber were made by pressurization with air in increments before each decompression step so that, following each decompression step, the P_{O_2} of the chamber would again approximate the 2.5-p.s.i. control levels (Figure 1b). In the 36-p.s.i.g. experiment, the decompression was at a slow, steady rate; and no compensation for the declining P_{O_2} was made (Figure 2b). The aim of both of these experiments was to assess the effects of pressurization without increase in P_{O_2} on 30-minute survival of lethally injured guinea pigs; and, in both experiments, mortality occurring beyond 30 minutes was considered to be biased because of unacceptable effects of the decompression.

Unexposed controls of both species were subjected to the same treatment schedules as the experimental animals, and none of these exhibited any ill effects from the treatment during the primary periods of interest as reported in this study.

Physiological Monitoring

Lead II ECG traces were recorded from rabbits before and at intervals after blast exposure.

Respiratory rates were obtained by visual monitoring of the rabbits.

RESULTS

Effects of Hyperoxia Versus Hyperbaric Pressure

The results of the initial guinea-pig experiments presented in table I and illustrated in figures 1 through 4 provided clear indications of the following:

1. Animals receiving treatment involving hyperbaric oxygenation exhibited marked increases in survival times, which were dependent upon the P_{O_2} of the treatment environment. However, for the treatment and decompression times used in these initial experiments, they did not exhibit increases in overall survival compared with that of untreated controls (cf., Figures 1a, 2a, 3b, and 4).

2. Animals receiving pressure treatment without increase in oxygen tension exhibited time-mortality curves which were very close to those of the untreated controls (Figures 1b and 2b). Thus, pressurization without increase in oxygenation was totally ineffective as modes of treatment in these studies.

3. Animals receiving treatment with 100-percent O_2 for 4 hours at normal ambient pressure exhibited increased survival until near the end of the treatment period and reached the control level of lethality by 3-1/2 hours post-shot, and they had a sharp increase in mortality above the level of the controls within 15 minutes after removal from the oxygen treatment chamber (Figure 3a).

4. The differences in survival, during the 30-minute hold-period, between the treatment groups and untreated controls were significant at the 95-percent confidence level in only the group illustrated in figure 1a ($P = .004$) which were pressurized to 72 p.s.i.g. with air (P_{O_2} = 17.5 p.s.i.a.). However, this difference in survival in the group having the next highest P_{O_2} (12 p.s.i.a.), those pressurized with air plus O_2 to 36 p.s.i.g. (Figure 3b), approached significance ($P = .06$). The mortality in both of these treatment groups reached the control levels by 2-1/2 hours post-shot.

TABLE I

EFFECTS OF HYPERBARIC TREATMENT AND OXYGEN THERAPY ON RESPONSE OF GUINEA PIGS TO AIRBLAST

Group No.	No. of Animals	Treatment	Time								
			Rise, Sec.	Hold, Min.	Decompression, Min.	Total Treatment, Min.	Survival				
							30 Min.	1 Hr.	2 Hrs.	5 Hrs.	24 Hrs.
1	10	12 p.s.i.g. Air (P_{O_2} = 5 p.s.i.)	10	30	10	40	7/10 70%	4/10 40%	4/10 40%	4/10 40%	1/10 10%
2	10	36 p.s.i.g. Air (P_{O_2} = 10 p.s.i.)	30	30	30	60	8/10 80%	8/10 80%	8/10 80%	4/10 40%	4/10 40%
3	10	72 p.s.i.g. Air (P_{O_2} = 17.5 p.s.i.)	60	30	50	80	10/10 100%	9/10 90%	5/10 50%	2/10 20%	2/10 20%
4	10	36 p.s.i.g. Air + O_2 (P_{O_2} = 12 p.s.i.)	30	30	30	60	9/10 90%	8/10 80%	6/10 60%	3/10 30%	2/10 20%
5	10	100% O_2 (P_{O_2} = 12 p.s.i.)	--	--	--	240	8/10 80%	8/10 80%	7/10 70%	2/10 20%	1/10 10%
6	10	36 p.s.i.g. N_2 + Air (P_{O_2} = 2.5 p.s.i.)	30	30	30	60	7/10 70%	5/10 50%	4/10 40%	3/10 30%	2/10 20%
7	10	72 p.s.i.g. N_2 + Air (P_{O_2} = 2.5 p.s.i.)	60	30	50	80	5/10 50%	3/10 30%	2/10 20%	1/10 10%	1/10 10%
8	58	Controls (P_{O_2} = 2.5 p.s.i.)	Airblast Only				33/58 57%	30/58 52%	29/58 50%	28/58 48%	18/58 31%

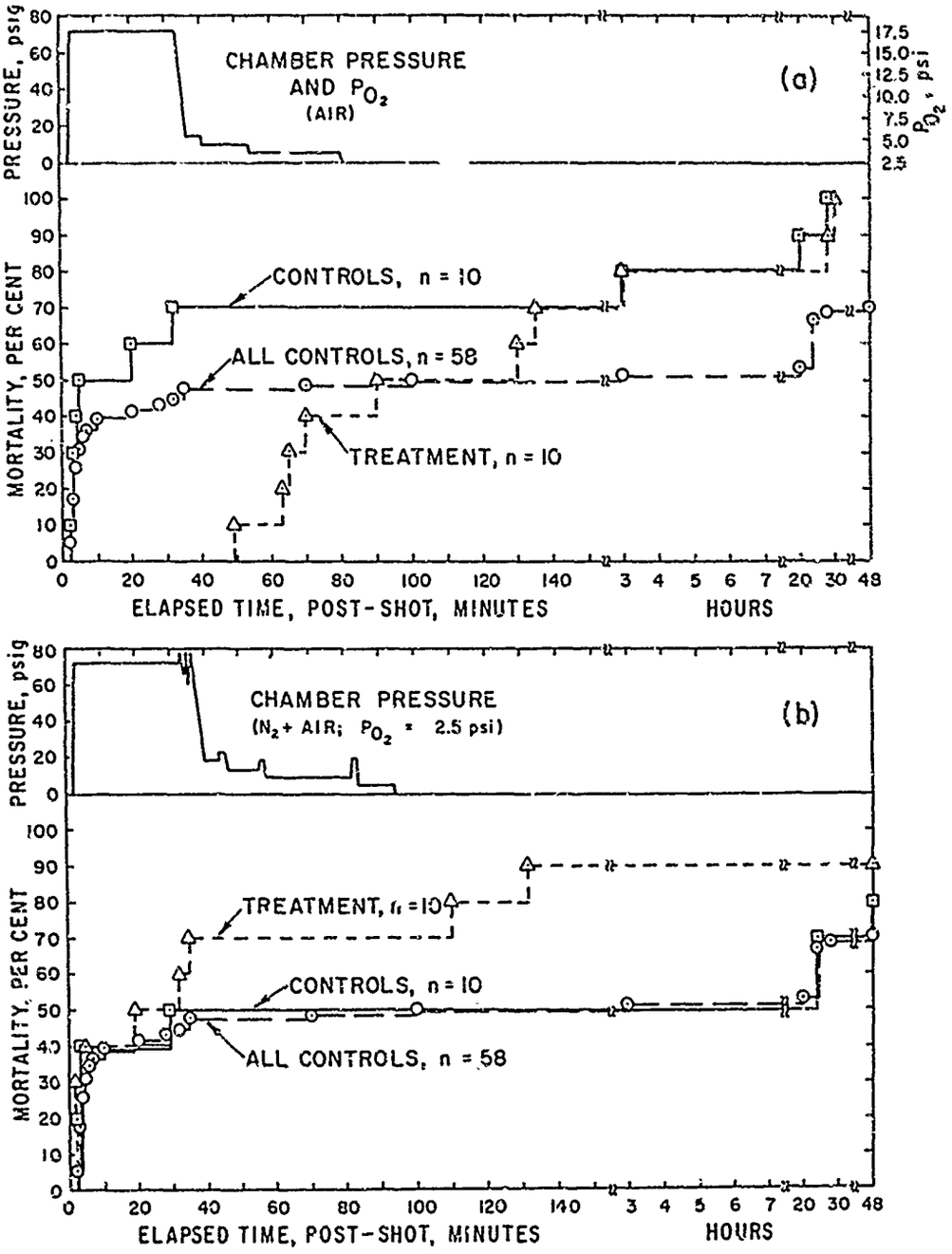

Figure 1. --Comparison of Effects of Pressurization to 72 p.s.i.g. With Increase in P_{O_2} (Figure (a)) vs. Pressurization With No Increase in P_{O_2} (Figure (b)) on Survival of Guinea Pigs Exposed to Airblast.

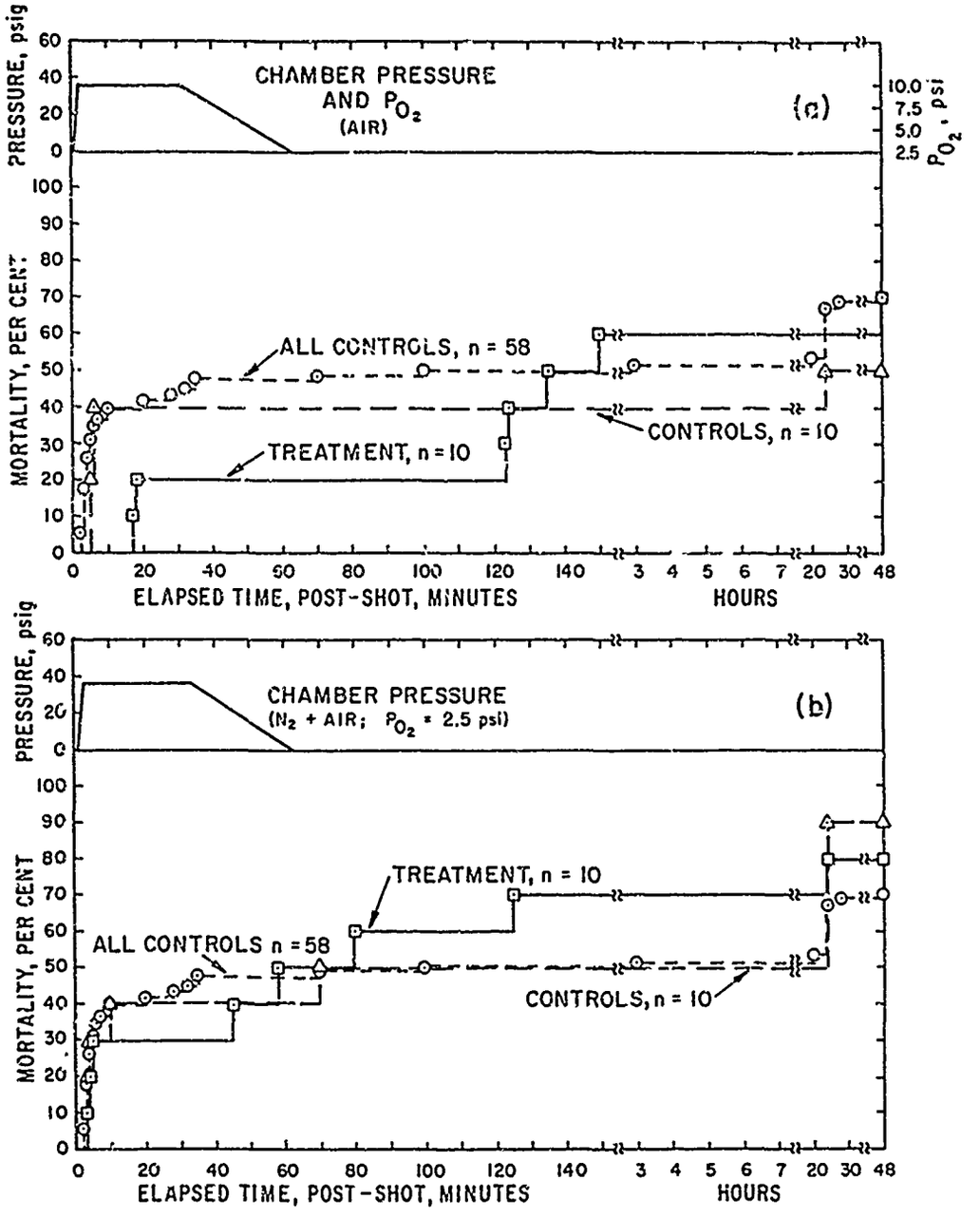

Figure 2. --Comparison of Effects of Pressurization to 36 p.s.i.g. With Increase in P_{O_2} (Figure (a)) vs. Pressurization With No Increase in P_{O_2} (Figure (b)) on Survival of Guinea Pigs Exposed to Airblast.

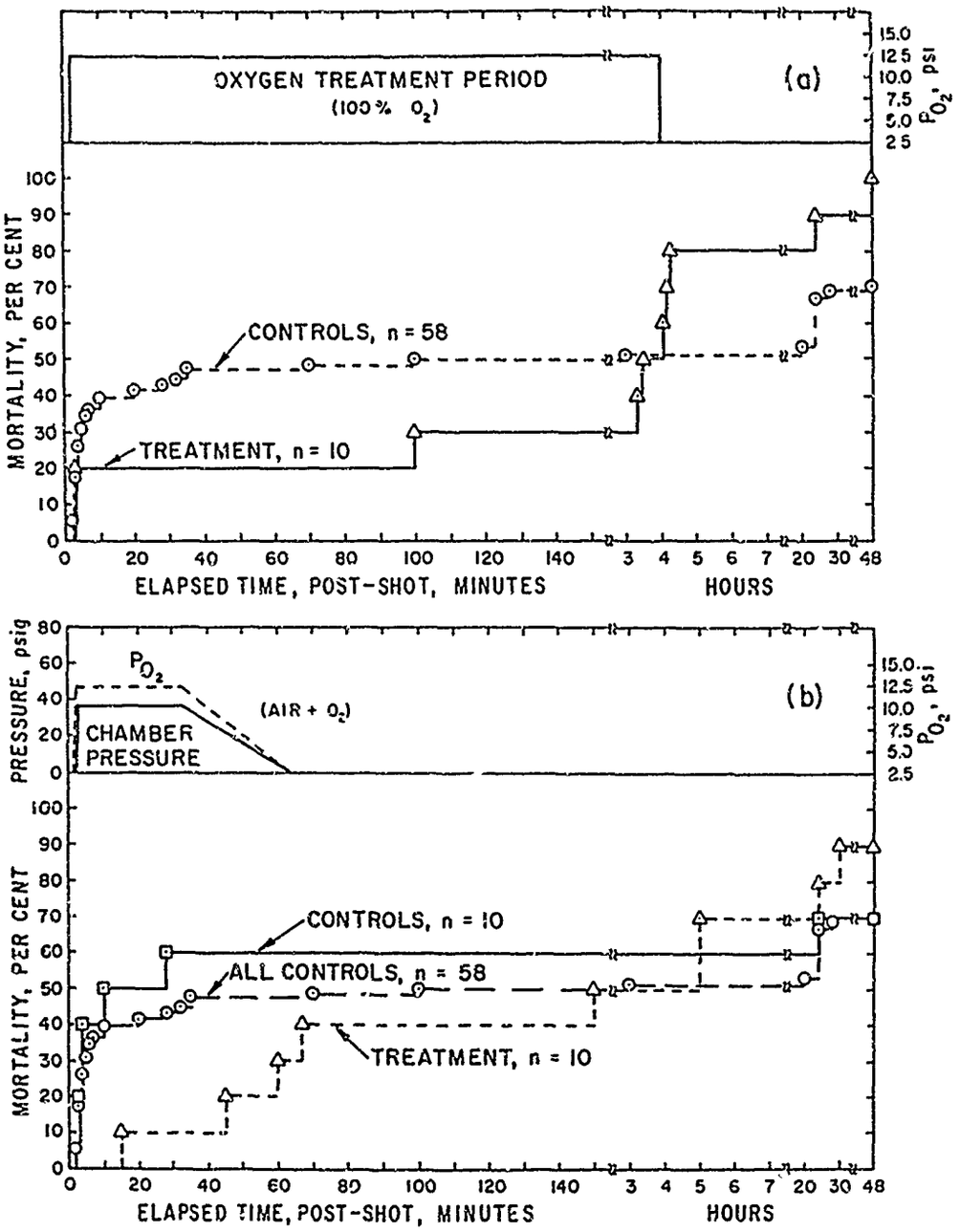

Figure 3.--Comparison of Effects of Oxygen Treatment (P_{O_2} = 12 p.s.i.) Without Pressurization (Figure (a)) vs. Oxygen Plus Pressurization to 36 p.s.i.g. (Figure (b)) on Survival of Guinea Pigs Exposed to Airblast.

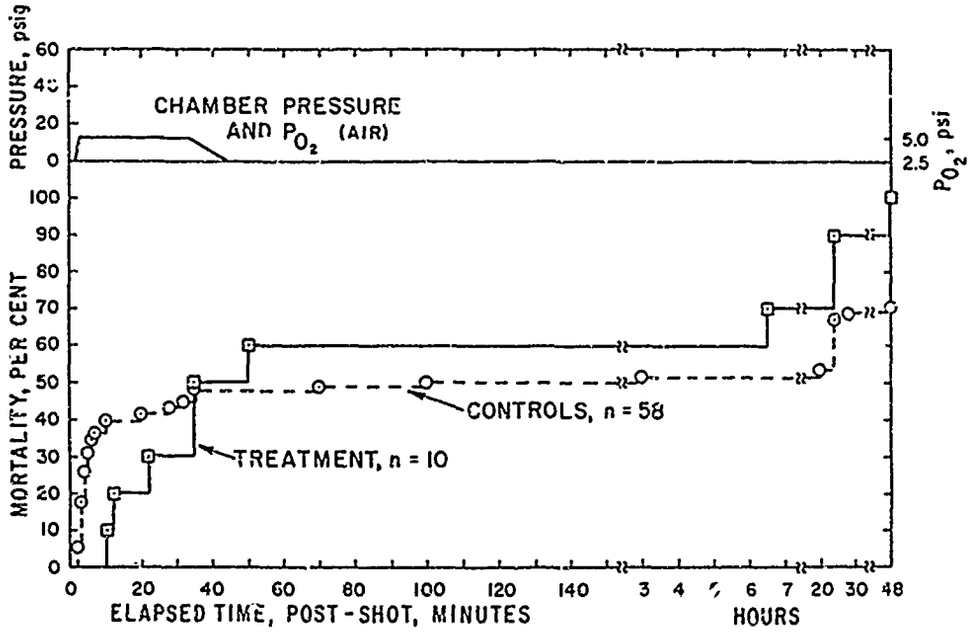

Figure 4.--Effects of Hyperbaric Treatment at 12 p.s.i.g. on Survival of Guinea Pigs Exposed to Airblast.

Effects of Prolonged Hyperbaric Treatment

The pressure-time treatment profiles utilized in the rabbit experiments and the time-mortality curves for the untreated blast control and the two treatment groups are illustrated in Figures 5a and 5b. The mortality in the untreated controls reached 35 percent within 15 minutes after blast exposure and climbed to a maximum of 59 percent by 24 hours. There were no deaths in either of the two treatment groups, and the differences in 14-day survival between the treatment groups and controls were significant with probabilities of .02 and .03 for experiments, group A and B, respectively.

Effects of Hyperoxia on Respiration in Blast Injury

Changes in respiratory frequency for the blast controls and two treatment groups of rabbits are illustrated in Figure 6a. The preshot respiratory frequencies for 10 animals ranged from 86 to 121 percent of the mean value. Presented in the lower part of Figure 6a are mean respiratory rates expressed as a percent of the preshot mean for animals in the two treatment groups and controls which survived longer than 1 hour. The blast controls exhibited post-exposure increases in respiratory frequency which reached a peak within 30 minutes post-shot. In both of the treatment groups, the mean respiratory frequency remained near the preshot level from 10 minutes post-shot throughout the treatment period.

Effects of Hyperbaric Oxygenation on Heart Rate in Blast Injury

The data plotted in Figure 6b show mean changes in heart rate following blast injury in rabbits surviving longer than 10 hours after exposure. The figure summarizes the heart rate changes which are expressed as a percent of the preshot mean for six animals receiving hyperbaric treatment with air at 72 p.s.i.g. (P_{O_2} = 17.5 p.s.i.a.), one animal pressurized with air plus oxygen at 15 p.s.i.g. (P_{O_2} - 17.5 p.s.i.a.), and five untreated controls from which ECG traces were recorded.

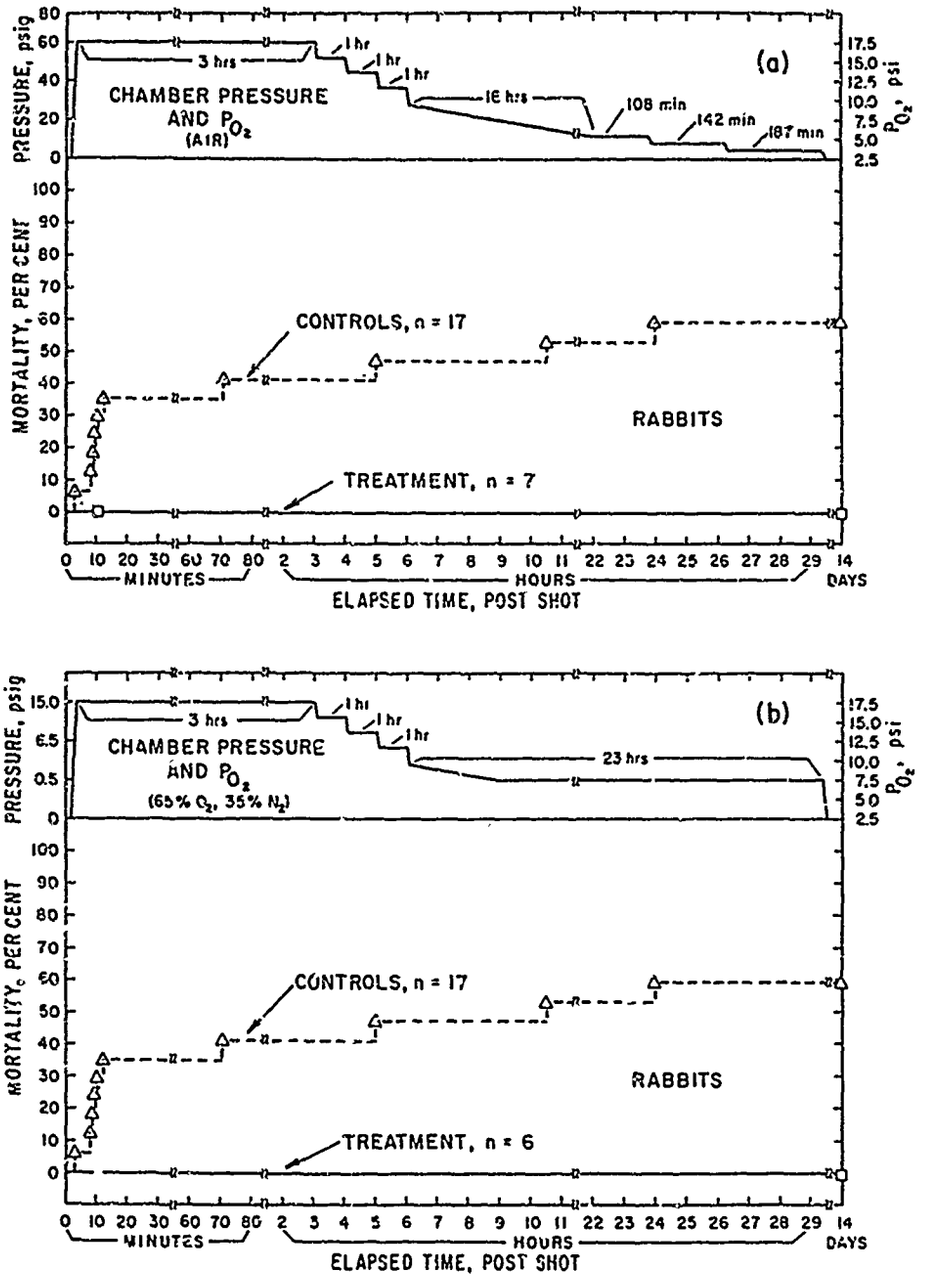

Figure 5.--Effects of Prolonged Hyperbaric Treatment With Air (a) at 72 p.s.i.g. (P_{O_2} = 17.5 p.s.i.a.) or a Gas Mixture (b) of 65-Percent O_2, 35-Percent N_2 at 15 p.s.i.g. (P_{O_2} = 17.5 p.s.i.a.) on Survival and Recovery of Rabbits Exposed to Airblast.

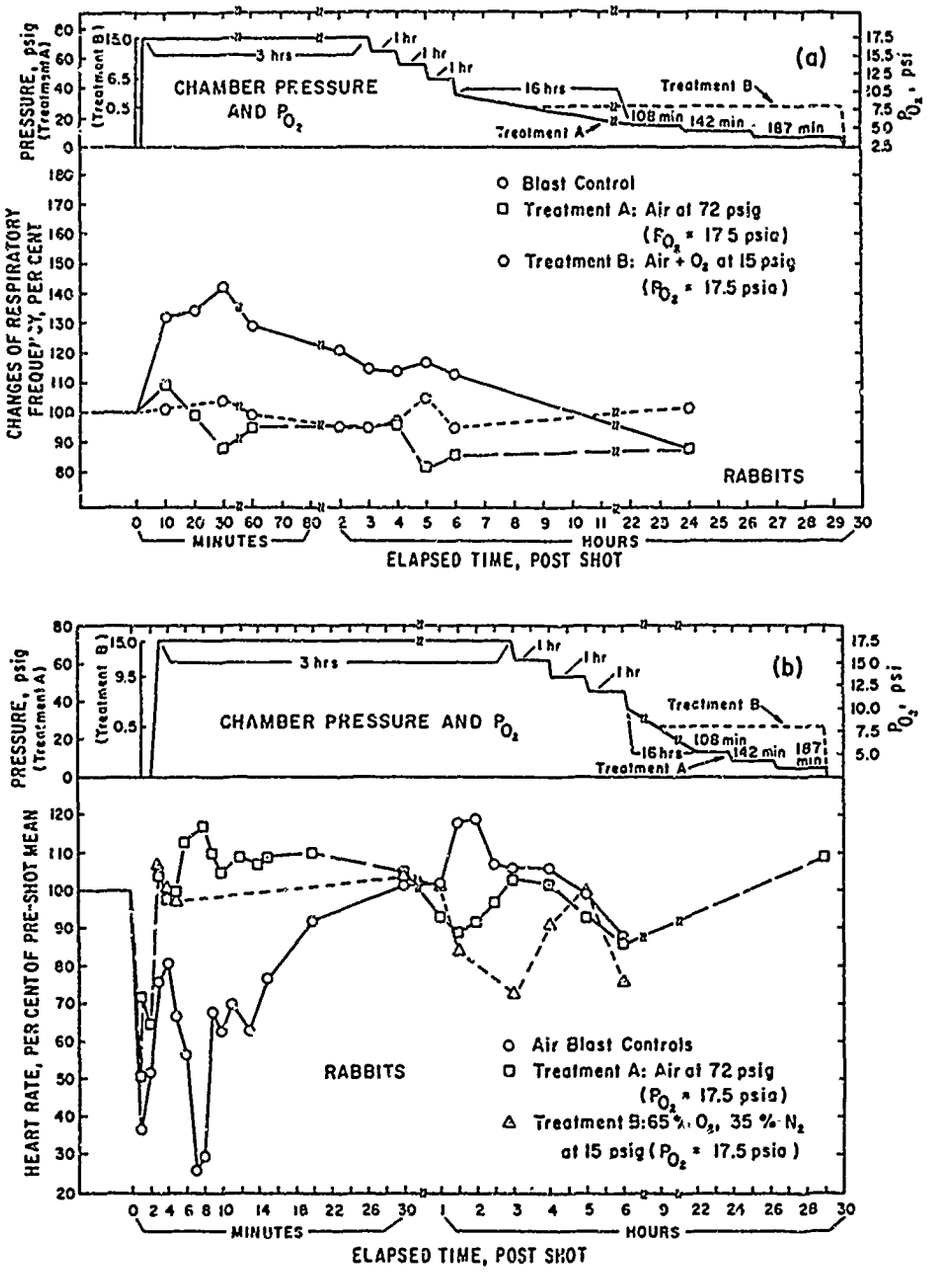

Figure 6.--Effects of Two Modes of Prolonged Hyperbaric Treatment on Respiratory Frequency (a) and Heart Rate (b) in Blast-Injured Rabbits.

The animals exhibited an initial post-exposure bradycardia with recovery followed by tachycardia, and then a general reduction in heart rate occurring 6 hours after exposure. The recovery from the initial bradycardia and the subsequent tachycardia occurred much earlier in the animals receiving treatment with hyperbaric oxygenation than in the untreated controls. The magnitude of the tachycardia was somewhat less and its duration was much less in the animals receiving treatment than in the controls. The animals in treatment group A exhibited a moderate reduction in heart rate during the last 2.5 hours of the initial 3-hour hold-period at 72 p.s.i.g.

Electrocardiogram

Major ECG changes observed in a control fatality, control survivor, and survivors in treatment groups A and B are illustrated in Figures 7 through 10, respectively. In the first few minutes after exposure, most of the rabbits exhibited various degrees of sinus bradycardia and arrythmia (Figures 7b, 8b-e, and 9b), sometimes with intervening ventricular extrasystolies (Figure 7d) or ventricular tachycardia (Figure 10b-d) and increased amplitude of the T-wave (Figures 7b and 9c). A control, 12-minute fatality, exhibited a transitory inversion of the T-wave following a convulsive seizure which occurred 4 minutes post-shot, after which there developed an increasing amplitude and high takeoff of the T-wave (injury potential), increasing P-R interval, anoxic bradycardia, and progressive heart block (Figure 7).

In a control survivor, the initial bradycardia persisted with gradual improvement for the first 18 minutes following exposure, after which the animal had a convulsive seizure followed by tachycardia. The animal then became comatose, but began to recover 4 or 5 minutes later. By 1-hour post-shot, the animal was alert, and the ECG revealed only a sinus tachycardia and a marked depression of the S-wave (Figure 8).

The various pathologic, ECG signs generally reverted to normal much more rapidly in the animals receiving hyperbaric oxygen treatment than in the controls. For example, the initial sinus bradycardia and arrythmia, with

NOTES FOR FIGURE 7

Air embolism found in peripheral and cerebral arteries, but none in the coronary arteries. ECG Lead II: 25 small divisions per second.

(a) Preshot: 223 beats per minute.

(b) Two minutes post-shot. Blast reflex bradycardia and increased T-wave amplitude: 81 beats per minute.

(c) Four minutes post-shot, during convulsions: 120 beats per minute.

(d) Six minutes post-shot after convulsions have subsided. Inversion of T-wave and intermittent ventricular extrasystoles (VES): 100 beats per minute.

(e), (f), and (g) Six and one-half to 7 minutes post-shot. Progressive reversion and increasing positive T-wave amplitude: 150-180 beats per minute.

(h) and (i) Nine minutes post-shot following cessation of respiration. Development of increasing injury potential (elevation of RS-T) and progressive increase in P-R interval.

(j), (k), and (l) Eleven and 12 minutes post-shot. Development of complete A-V block and ventricular arrest.

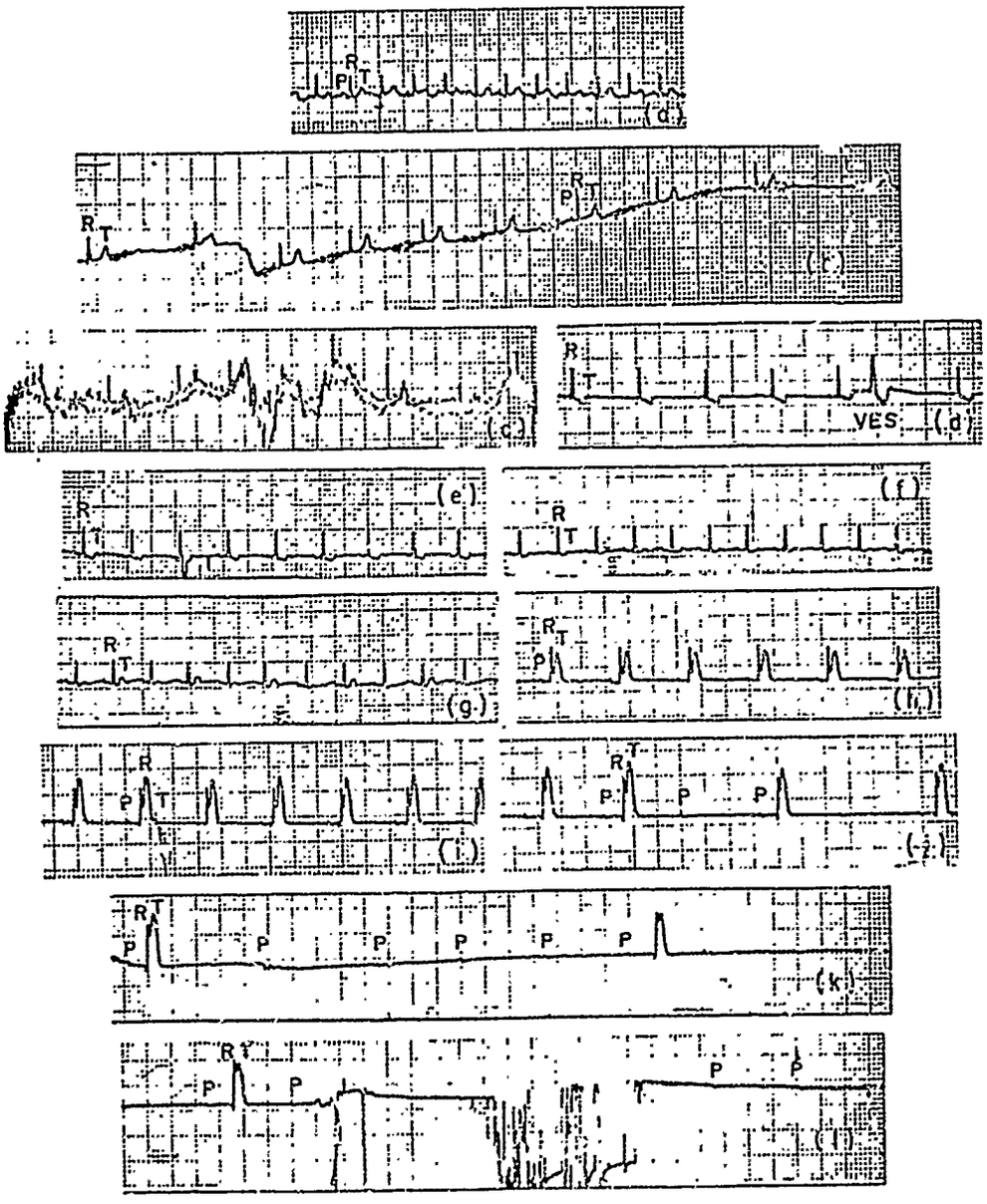

Figure 7. --Air Blast Control Rabbit B-30, 12-Minute Fatality, Reflected Air Pressure = 31 p.s.i.g.

NOTES FOR FIGURE 8

ECG Lead II: 25 small divisions per second.

(a) Preshot. Rate, 280 beats per minute.

(b) Five minutes post-shot. Sinus bradycardia (124 beats/minute) and arrythmia.

(c) A few seconds later. Pronounced bradycardia (52 beats/minute) with increase in P-R interval.

(d) Seven minutes post-shot. Recovery of normal P-R interval; heart rate 70 per minute.

(e) Nine minutes post-shot. Increasing amplitude of S-wave. Rate: 100 per minute.

(f) Eighteen minutes post-shot. Reduction in amplitude of QRS. Rate: 210 per minute.

(g) Twenty-six minutes post-shot following convulsive seizures. Tachycardia (310 beats/minute) with increase in amplitude of QRS. One minute later, the animal became comatose, but remained so for only 4 or 5 minutes.

(h) One hour post-shot. Animal alert. Depressed S-wave, normal rhythm. Rate: 305 beats per minute.

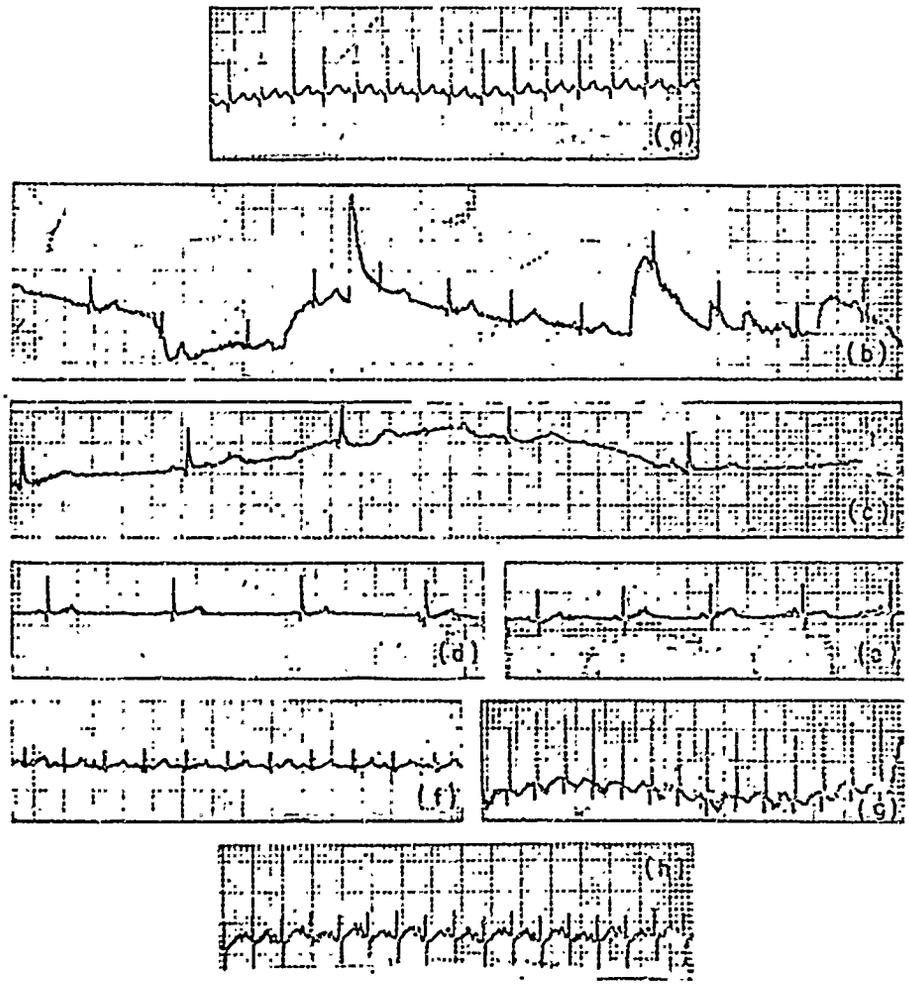

Figure 8.--Airblast Control Survivor Rabbit R-19, Exposed to Reflected Pressure of 28 p.s.i.g.

NOTES FOR FIGURE 9

ECG Lead II: 25 small division per second.

(a) Preshot. Heart rate = 254 beats per minute.

(b) One minute post-shot. Sinus bradycardia (115 beats/minute) and arrythmia.

(c) Two and one-half minutes post-shot. During pressurization when the chamber pressure has reached 40 p.s.i.g. Increasing heart rate (190 beats/minute), high amplitude T-wave.

(d) Five minutes post-shot after 2 minutes at 72 p.s.i.g. Reduction in amplitude of the T-wave to preshot level. Heart rate = 220 beats per minute.

(e) Fifty minutes post-shot. Slight reduction in amplitude of the QRS. Rate and rhythm near the preshot levels (240/minute).

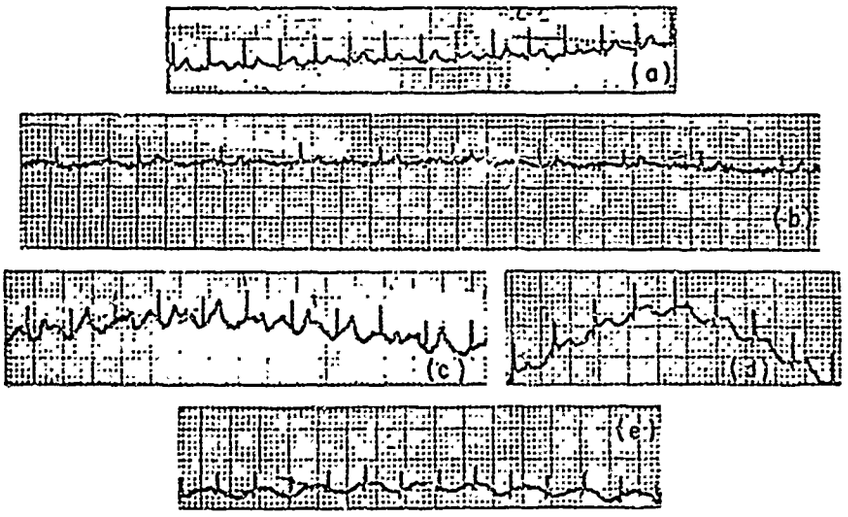

Figure 9.--Rabbit R-9. Hyperbaric Treatment With Air at 72 p.s.i.g. (P_{O_2} = 17.5 p.s.i.a.). Reflected Shock Pressure = 26.1 p.s.i.g.

NOTES FOR FIGURE 10

ECG Lead II: 25 divisions per second, 100 μv. per division for all traces except (f) is 200 μv. per division.

(a) Preshot. Heart rate = 276 beats per minute.

(b) Two minutes post-shot before beginning treatment. Ventricular tachycardia (294/minute) with varying numbers of ventricular extrasystolies (VES) occurring between normal beats (NB).

(c) Two and one-half minutes post-shot during pressurization. Ventricular rate = 304 beats per minute.

(d) Three minutes post-shot after reaching pressure treatment level (15 p.s.i.g., P_{O_2} = 17.5 p.s.i.a.). Ventricular rate = 310 beats per minute.

(e) Five minutes post-shot, 1:1 normal beats to ventricular extrasystolies. Ventricular rate = 268 beats per minute.

(f) Thirty minutes post-shot. Recovery of normal rhythm. Rate = 286 beats per minute.

(g) Ninety minutes post-shot. Rate = 232 beats per minute. The rate declined to 202 beats per minute by the end of the 3-hour treatment hold-period, then increased to 276 beats per minute during the second decompression step, and had declined to 209 beats per minute by the end of the third decompression hold-time (6 hours post-shot). The rhythm and pattern remained normal.

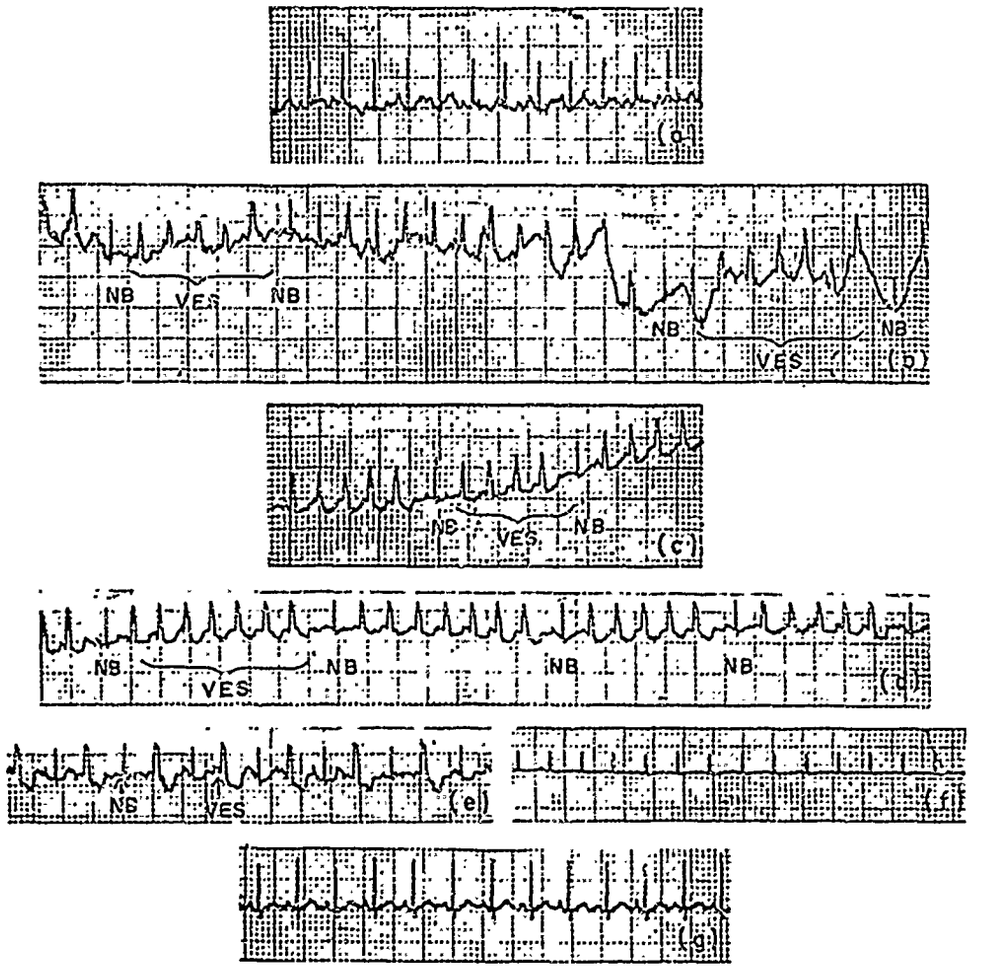

Figure 10.--Rabbit R-34. Hyperbaric Treatment With 65-Percent O_2, 35-Percent N_2 at 15 p.s.i.g. (P_{O_2} = 17.5 p.s.i.a.) Following Exposure to a Reflected Shock Pressure of 30.3 p.s.i.g.

intervening ventricular tachycardia, seen 2 minutes post-shot in a rabbit in treatment group B had almost completely subsided by 5 minutes post-shot, some 2 minutes after reaching the pressure treatment level. The rate, rhythm, and waveforms were normal by 30 minutes post-shot, after which the heart rate slowly declined to 202 beats per minute (75 percent of preshot) by the end of the 3-hour hold-time, increased to the preshot level during the early phases of the decompression and declined to 209 beats per minute by the end of the third 1-hour decompression step (Figure 10). The ECG rhythm and pattern remained normal and these changes in rate evidently were responses of the animal to the P_{O_2} of the gases in the hyperbaric chamber (Figure 6b).

Prolonged Hyperoxia in Treatment of Guinea Pigs

The guinea-pig experiment illustrated in Figure 11a was designed to duplicate the P_{O_2} changes with time utilized in the latter of the two rabbit experiments (Figure 5b). To provide additional information on the effects of O_2 concentration (F_{O_2}), however, 100-percent O_2 was utilized for the first 6 hours of the 29-hour treatment schedule and 65-percent O_2, 35-percent N_2 for the remaining 23 hours of the schedule. The results shown in the time-mortality curves in Figure 11a indicated that the treatment produced a marked increase in the survival times of the animals with no overall increase in recovery compared to that of the untreated controls. However, when the initial P_{O_2} of 24 p.s.i. was utilized, as illustrated in the time-mortality curves in Figure 11b, there were no deaths among the eight treated animals during the 29-hour treatment period, and only one death at 4 days post-shot during the 14-day period of observation. The difference in 48-hour survival between the treated and untreated control group was significant at the 98-percent confidence level ($P = .016$); whereas, at 14 days, the difference in survival of the two groups was only significant at a probability level of .058.

Pathological Findings

The types of lesions seen at autopsy in the fatalities in both the treatment and control groups were similar to those which have been previously described

NOTES FOR FIGURE 11

F_{O_2} = fractional concentration of O_2 in chamber.

P_{O_2} = partial pressure of O_2 in chamber.

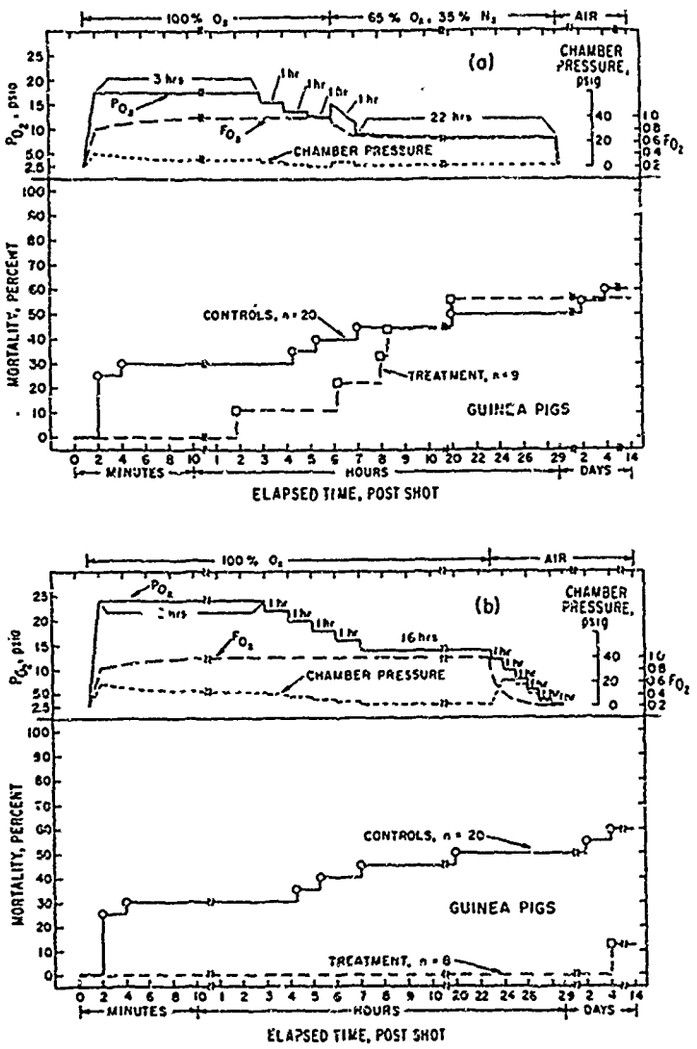

Figure 11.--Comparative Effects of Prolonged Treatment With 100-Percent O_2 at an Initial P_{O_2} of 17.5 p.s.i.a. and a Chamber Pressure of 5.5 p.s.i.g. (a) or at a P_{O_2} of 24 p.s.i.a. with O_2 at a Chamber Pressure of 12 p.s.i.g. (b) on Survival and Recovery of Guinea Pigs Exposed to Airblast.

in the literature on blast biology.[2, 3, 15, 18] They include massive pulmonary hemorrhage and edema, occasional hemothorax or pneumothorax, hemorrhagic spots on the walls of the gastrointestinal t.. ., and occasional hemoperitoneum with ruptured liver or spleen. Animals that died after several hours in both the treatment and control groups generally exhibited a more extensive development of pulmonary hemorrhage and edema than those that died within a few minutes after exposure. Also, there were no gross differences in the nature or extent of the lesions seen in survivors in the treatment and control groups.

DISCUSSION

In these experiments, pressurization of guinea pigs with nitrogen to 36 or 72 p.s.i.g. with the P_{O_2} retained at the normal ambient level failed to effect any change in survival of lethally blast-injured animals; whereas pressurization with air resulted in increases in survival time which could be related to the elevation of the P_{O_2} of the treatment chamber gas. This may indicate that factors other than air embolism are also contributory to early lethality following blast injury. Pressurization at a constant P_{O_2} level achieves only two of the three major aims of therapy for air embolism; i.e., decrease in volume and increase in the rate of resolution of the gas bubbles, while the third aim, maintenance of tissue oxygenation, is not benefited by this mode of treatment.

In contrast to the above, all methods of treatment involving elevation of the P_{O_2} of the inspired gases resulted in increases in the survival times for guinea pigs and an increase in survival and recovery of rabbits which received prolonged treatment at an initial P_{O_2} level of 17.5 p.s.i.a. Similar results were achieved by prolonged treatment of guinea pigs at a P_{O_2} of 24 p.s.i.a.

The rapidly developing pathophysiologic changes occurring after blast injury are complex and are probably highly interrelated. In concert, they may result in early or delayed lethality. These have previously been described by a number of investigators and will be discussed only from the standpoint of the effects of hyperbaric oxygenation in the treatment of such injuries. For convenience, they may be divided into two categories: (1) the immediate direct responses of the body to the blast pressure wave; and (2) secondary or delayed physiologic responses which accrue from these initial reflex or patho-anatomical changes.

Among the immediate effects are the occurrence of pronounced bradycardia and pathologic ECG changes produced by the direct effects of the blast pressure pulse acting on the heart, lungs, and carotid sinus.[5, 7] This is accompanied by a precipitous drop in the arterial blood pressure, an increase in the amplitude, and often an increase in the average blood pressure of the right ventricle.[2]

These initial, blood pressure changes in the pulmonary artery and right ventricle are apparently due to increased pulmonary-vascular resistance caused by mechanical and reflex mediated factors in the blast-injured lung.[5]

Within a few minutes after the initial blast responses of the cardiopulmonary vascular system, there may follow a reduction in the cardiac output due to inhibited pulmonary venous return to the left heart and progressive hypoxia due, in large part, to an increase in the venous admixture because of continued flow of venous blood through blast-injured, nonventilated regions of the lungs.[2, 13] Thus, the arterial O_2 saturation of the blood is decreased.[2] This is frequently accompanied by tachycardia and tachypnea.[2, 5] In addition to this, there are localized anoxic and ischemic effects caused by the occurrence of arterial air embolism which may have catastrophic consequences if they involve the circulation to the heart or central nervous system.

These early effects may be complicated by progressive development of pulmonary hemorrhage and edema, pulmonary hypertension, dilatation of the right heart, increasing anoxemia, acidosis, and hypercapnia which may reach proportions that are incompatible with life.[2, 11, 13, 15]

That the sequence of pathophysiologic changes described above may be reversed or reduced to levels compatible with survival and recovery of animals receiving appropriate hyperbaric oxygen treatment was indicated by the results of the experiments with rabbits and the last two guinea-pig experiments which were described in this study. This is suggested not only by the fact that all rabbits receiving treatment for 29 hours at an initial P_{O_2} of 17.5 p.s.i.a. survived and recovered from their injuries, whereas the untreated controls, which were initially exposed to the same shock pressures as the treated animals, exhibited a mortality of about 60 percent within 24 hours after exposure, but also by the fact that there were differences in changes in respiratory frequency and heart rate which are illustrated in Figure 6. Additionally, the pathologic changes in the ECG more quickly reverted to normal in animals receiving treatment than in the controls.

All of the foregoing point to the importance of oxygen therapy in the treatment of primary blast injury to the lungs. However, the question of whether the administration of 100-percent O_2 at normal ambient pressure is beneficial or harmful remains as an important problem. Mortality in guinea pigs treated with 100-percent O_2 for 4 hours post-shot reached the cumulative level for all controls by 3-1/2 hours post-shot and showed an additional 30-percent increase within 15 minutes after removal from the oxygen chamber (Figure 3(a)). But, in a subsequent experiment, when guinea pigs were treated with 100-percent O_2 at a partial pressure of 24 p.s.i.a. for 3 hours followed by a 26-hour decompression schedule, there were no deaths during the treatment period and only one death occurred after the animals were removed from the chamber. Thus, in the former experiment, the deaths that occurred during and following treatment apparently indicate that the P_{O_2} of 100-percent oxygen at normal ambient pressure was inadequate for the requirements of these severely injured animals and do not indicate that 100-percent oxygen at normal ambient pressure had marked deleterious effects.

In the guinea-pig experiment where the animals were pressurized with air to 72 p.s.i.g. (P_{O_2} = 17.5 p.s.i.a.), the deaths began at 49 minutes post-shot when the P_{O_2} of the chamber had dropped to levels below 5 p.s.i.a. during the decompression steps. One cannot entirely rule out the possibility that some of the deaths occurring during and following decompression in this experiment might have been due to decompression sickness for, although uninjured controls tolerate this decompression regime with no apparent effects, animals with severe blast injury to the lungs with attendant impairment of circulation and gas exchange may have a markedly reduced tolerance to such pressure changes; and one of the key principles of hyperbaric treatment for air embolism is that the decompression must be conducted at a much slower rate than that of decompressing from a dive.[23]

However, recent trends in the treatment for air embolism call for much shorter decompression times with intermittent breathing of O_2 and air during the decompression.[24] In a recently completed experimental study involving

observation of artificially induced cerebral air embolism through a cranial window in the dog, the investigators found that "bounce" dives to 165-foot equivalent depth (73.5 p.s.i.g.) for 10 minutes with decompression in accordance with the Standard Navy Decompression Table (at an ascent rate of 25 feet per minute with a 2-minute stop at 10 feet) resulted in complete resolution of the bubbles; and, in no case, was there a reappearance of the bubbles during or following the decompression.[25] In the aforementioned guinea-pig experiment, gas embolism was not detected at autopsy in any of the animals in the treatment group. Therefore, the deaths which occurred during and following decompression in this experiment can best be attributed to the reduction in P_{O_2} rather than a reappearance of air emboli or the development of decompression sickness.

Furthermore, the results of the guinea-pig experiment, in which the animals were treated with 100-percent O_2 for 23 hours at an initial P_{O_2} of 24 p.s.i.a. followed by a 6-hour treatment with hyperbaric air during the final decompression phases of the treatment, indicated that full recovery and survival of guinea pigs with lethal blast injuries can be achieved provided the P_{O_2} of the chamber gas is retained at an adequate level for a sufficient time.

With reference to the use of 100-percent oxygen, theoretical considerations lead one to believe that poorly ventilated alveolar segments containing pure oxygen would tend to become more atelectic because of cellular utilization of the oxygen than if they contained an oxygen-nitrogen mixture. As far as oxygen toxicity is concerned, recent studies of the pathophysiology of pulmonary oxygen toxicity of normal animals have indicated that toxic effects are independent of O_2 concentration and dependent solely on the P_{O_2} and the duration of exposure.[27] These investigators found that at a P_{O_2} of 1 atm at various O_2 concentrations, surfactant measurements and autofluorescence of alveolar lining membranes of rats or guinea pigs remained normal for the first 48 hours and became abnormal only just before death after 55 to 60 hours of exposure.

The P_{O_2} of the gases in the hyperbaric chamber in the rabbit experiment shown in Figure 5b was at levels above 8 p.s.i. for 29 hours. In the last

guinea-pig experiment (Figure 11b), the P_{O_2} was retained for 23 hours at P_{O_2} levels of 14 to 24 p.s.i.a. No evidence of O_2 toxicity was seen in these animals, and there were no apparent ill effects of the 100-percent O_2 concentration utilized in the guinea-pig experiment. In view of the evident importance of oxygen treatment, the problem of whether those with blast injury are more or less susceptible to O_2 toxicity than uninjured patients is of considerable interest.

Since O_2 toxicity is apparently not only governed by alveolar O_2 pressures alone, but also by arterial P_{O_2},[26] and one would predict that the increased venous admixture resulting from continued perfusion of blast-injured, nonventilated regions of the lungs[13] might render such animals more resistant to oxygen toxicity than animals without such injuries. In any event, the beneficial effects of hyperoxia at the P_{O_2} levels for the treatment durations utilized in the rabbit and last two guinea-pig experiments in this study overrode any harmful effects of the elevated P_{O_2}.

Finally, the fact that the response of animals to hyperbaric treatment following blast injury is dependent upon the initial P_{O_2} and independent of the pressure in the chamber is very encouraging because, if the pressure required for treatment of blast injury can be minimized, the design problems in production of portable hyperbaric units for use in the field will be reduced; and there should be fewer complications during decompression phases of the treatment.

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